Comments for CBER FDAMA Section 406(b) Meeting - Docket 98N338B
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My name is Emily Rossiter. I have been working in the field of blood banking for over 25 years – first with the American Red Cross, then as an independent consultant for the last 15 years. I have never worked *for* FDA – but I've continuously been working *with* FDA, on the other side of the table. Today, I appreciate the opportunity to act as consultant to FDA CBER staff on reform and reinvention.

I am joined in these comments by the six companies listed on this first slide and six others, who support these comments but requested that their names be withheld. Some are clients, some are colleagues and friends. All support quicker patient access to improved blood products and technologies, through shorter review times at FDA and more constructive dialogue with CBER policy staff. These companies all make blood banking and plasma related products – drugs, devices, *in vitro* diagnostics – that are reviewed by CBER and have been outside user fee and fast track channels. They do not make licensed biological products, so their review times are not covered in the review time data you've seen from CBER.

I would like to highlight four areas today, specifically for the CBER blood applications audience, as you brainstorm ways to further improve performance and meet obligations under the new reform legislation. These areas are: review and response timetables; the extent and detail in reports and submissions; the integration of related submissions; and regulatory harmonization. Most of the suggestions can be implemented at a policy level – without changes to regulations. They stem from a philosophy that the quality of information coming into FDA is more important than the quantity, that time and predictability mean *everything* to companies in the blood bank field, and, that, faced with limited resources, further priority setting by CBER could redirect staff time and efforts in constructive ways.

First, and most importantly, review times for blood related drugs, devices and products need to be reduced significantly, across the board, if were are to get them to the patient. Six months should be the outside limit for any review cycle, not just fast track products. Taking more than six months, in a field as dynamic as blood banking, creates a self perpetuating problem. The information becomes out of date before it gets reviewed. This leads to amendments, review letters and response cycles, all while technology and FDA policy are further evolving. The best way to get out of this loop is to shorten the turnaround, so that expectations and technology can be synchronized.

Review times for responses to Warning Letters or other enforcement topics need goals too. If circumstances warrant an FDA enforcement letter or action, calling for a prompt response from industry, then review by FDA within 2-3 months would be reasonable, so that customers and patients who could benefit are not left in limbo.

Second, there are many areas of detail and traditional practices that will come up for scrutiny during your reinvention sessions, and I've listed some of my favorites on this slide. Let me first emphasize that I do not mean that we should reduce the level of detail available to FDA on site, at the manufacturing facility. These suggestions affect the amount of detail sent into FDA routinely for review, response and management. For example:

- Blood or plasma recalls – all recalls are not equal. Many blood or plasma recalls, involving only hypothetical risks, technical deviations, or small numbers of expired products, could be relegated to market withdrawal status.

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- Error and accident reporting -- Error and accident reporting is unique, in its implementation in blood establishments, and is over 20 years old. FDA has proposed extending error and accident reporting to hospital based transfusion services and recently highlighted its applicability to licensed *in vitro* diagnostic manufacturers. Before extending it, let's critically examine the historical experience with the current program -- has it served a critical role in the past 20 years? We may find that more recent surveillance programs, such as Medical Device Reporting and MedWatch, and the existence of industry-based quality programs for deviation tracking and trending, provide more modernized methods of getting useful information.
- Me too sites and products -- are another good area to reduce paperwork without reducing safety for blood donors or recipients. The addition of new apheresis collection sites or adding sites to make already approved blood components, in an organization which has proven itself, should not be a major task for FDA review. Similarly, the addition of modified blood products, such as irradiated or leukocyte reduced products should not be a major exercise by regulatory agencies. And by "major exercise," I mean prior approval supplements for each location, pre-approval inspections, etc.
- CBER staff have embraced the concept of report simplification and reduction -- trying to ease the process by which changes can be made to existing products. But more is needed. More downgrading of changes to 30 day notice and annual report is both possible and necessary, to allow CBER staff to focus on larger, more critical issues.

Third, integration of approval processes for new blood product license supplements with drug and device clearances would speed technology improvements to patients. This slide will help me explain what I mean. The top three boxes on this slide represent the technologies used to collect and process blood or plasma from donors. Several companies make blood processing solutions and disposable plastic bag sets which are used along with filters, separators, expressors, etc. (instruments) to make blood products for transfusion, depicted in the bottom three boxes. Typically, the storage solution, in the upper left of the slide, undergoes a drug approval process (NDA or ANDA) and the processing containers, along with any related instruments, undergo device premarket submission. A pre-approval inspection may also be required. Obtaining premarket clearances for these technologies, in recent times, has taken anywhere from 2 years to over 10 years -- whether they are new generations of technologies, "me too," or modest improvements.

If these solutions and devices are destined for use directly in patient care, or in unlicensed blood banks, these clearances are the only ones needed from FDA. But if the same solutions or sets are to be used in a licensed blood center and the blood products shipped in interstate commerce, we are only half way there. Another premarket approval and prelicense inspection cycle is often required, sometimes for each of the products on the lower slide, for each location of a licensed facility. This adds another few years delay in the availability of the resulting blood product, interstate. This means that patients served by unlicensed, intrastate blood banks can benefit from new technologies several years before patients served by licensed blood facilities.

Over the years, FDA has used guidance documents and notifications to facilitate licensed blood center use of new technologies, for example in infectious disease testing; there is room to expand this practice where a technology has a proven track record for many years or where the benefits outweigh the risks.

Finally, further harmonization will help blood technology improvements reach the patient. Areas where CBER, CDRH, or CDER regulate similar technologies for similar uses should be analyzed and the lowest common denominators found for a more unified approach to regulatory policy and enforcement. These areas include parenteral solutions, instruments, *in vitro* diagnostics, single use disposable products,

and computer software programs. Differences between the regulatory policies for these products should be held to scrutiny, perhaps by external advisory groups, and the differences eliminated unless they can be adequately defended by science, not emotion.

FDA's ongoing efforts at international harmonization are appreciated. In the area of blood banking, an analysis of the risks and benefits of the European Community's policy toward blood processing solutions – as device accessories – versus the FDA's "drug" approach might reveal some useful information during reinvention deliberations. Ultimately, international harmonization efforts should continue until a single, global dossier is recognized for all blood and plasma products, drugs, and devices.

Before closing, I also want to recognize some of the recent successes of FDA and CBER. First, the FDA Home Page and internet sites have greatly improved industry's ability to stay up to date and monitor developments in a timely fashion. Continuing efforts to enhance the information, adding search capability and better links and organization, are very useful and greatly appreciated. Second, to CBER blood staff, the open door and open telephone line policies that you have tried to maintain are absolutely essential to a safe blood supply. It has been difficult to accommodate the mounting requests that have resulted from your current workload, but it is important that you know that each personal contact with industry is regarded as a precious investment in the future. Thank you.

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Blood Technology Reform

- Review and Response Timetables
- Reports and Submission Detail
- Approval process integration
- Harmonization – internally and externally

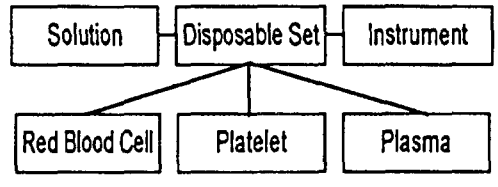
Review and Response Times

- 6 mo. max for original applications
  - 510k
  - NDA/ANDA
  - BLA
- 3 mo. max for supplements
- 2-3 month max for CBER enforcement reviews

Details, Details, Details

- Downgrade many blood/plasma recalls
- Revisit the value of E & A reports
- Relegate "me too" sites and products to 30 day notice or annual reports
- Down grade reporting requirements for changes to existing sites and products

Integrate NDA, 510k & BLA



Harmonize

- Blood manufacturing versus therapy
  - blood separators, filters
  - *in vitro* diagnostics (donor vs patient)
  - software programs
- Could blood solutions be treated as device accessories?
- Single, global dossier

Kudos

- Exploitation of internet
  - Searchability
  - Links & Organization
- Open doors and telephone lines

Blood Technology Firms

- Haemonetics Corporation
- COBE BCT, Inc.
- Pall Corporation
- Terumo Medical Corporation
- Genetic Testing Institute, Inc.
- Gamma Biologicals, Inc.
- Six other diagnostics, software, and blood solutions manufacturers